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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,127	10/30/2001	Rekha G. Panchal	P03357US2	1718

22885 7590 05/12/2005

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,127	PANCHAL ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 32-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-7,14-18,20 and 21* is/are allowed.

6)☒ Claim(s) *8-13,19,22-27 and 32-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is in response to the communication filed 2-21-05.

2. Claims 1-27, 32-39 are pending in the instant application.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Maintained Rejections

4. Claims 8-13, 22-27, and 32-39 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practicing the claimed invention *in vitro*, does not reasonably provide enablement for practicing the full scope of the claimed invention *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the same reasons set forth in the Office Action mailed 10-21-04.

Applicant's arguments filed 2-21-05 have been fully considered but they are not persuasive.

Applicants disagree with the Examiner's suggestion that the cited references support the position that the application of tRNA suppressors are highly unpredictable and would not be effective suppressors. According to Applicants, the examiner has not considered the articles as a whole, Applicants argue that when the articles are read in their entirety the authors are merely stating a well known fact that 3' codon context plays a role in the efficiency of human nonsense suppressors, and that neither reference provides any evidence that extrapolation from *in vitro* data to *in vivo* data is unpredictable. Moreover, According to Applicants, the articles, when read

as a whole, actually teach the potential usefulness of tRNA suppressors in cells, and more importantly fail to provide any reasonable basis to doubt the ability of the tRNA suppressors to read a nonsense codon and insert an amino acid in a nascent polypeptide in cells as observed in the instant invention.

Contrary to Applicant's assertions, the very fact that there is variability associated with the ability of a tRNA suppressor to function because of the nucleotide sequence context of the 3' codon, suggests that there is certainly a significant level of unpredictability associated with the behavior of a tRNA suppressor *in vitro* in comparison to its ability to function within the genome of a cell *in vivo*. Moreover, contrary to Applicant's assertions, the Atkinson et al reference not only teaches variability associated with 3' codon context, but further teach that the effectiveness of suppressors differ also with respect to which codons are being read and on the contexts in which termination signals lie. The claims read broadly on introducing any site-specific mutation into any translated protein, as well as correcting any genetic defect in an organism comprising administration of the array of tRNA constructs claimed. And, although the identity of the particular suppressor tRNA largely determines which amino acid is inserted, it remains uncertain what happens if products other than the target wild type gene product is generated.

On page 13 of Applicant's arguments filed 2-21-05 Applicants stated that the examiner described that Li et al. cite that one major concern for the use of tRNA suppressor in human gene therapy is their potential toxic effects. According to Applicants the Atkinson et al. reference addresses these concerns by stating that "in the case of gene therapy by a suppressor tRNA the level of tRNA could be adjusted so that the read-through by at a natural stop codon may be as little as 5-10%...Read-through of this intensity at natural termination codons, may not present so

drastic an outcome in the presence of 90-95% of correctly terminated polypeptide chains." However, contrary to Applicant's assertions, although Atkinson makes this statement, there is no guidance and/or instruction that would teach that skilled artisan how to level of tRNA could be adjusted to produce 90-95% of correctly terminated polypeptide chains. Moreover, it is noted that the above passage from the Atkinson et al. reference also questions whether or not a reduction in the level of read-through at natural stop codons by gene therapy would be sufficient to reverse a mutant phenotype. Furthermore, it is clear that at the time of the Atkinson et al. reference there was no clear guidelines associated with practicing gene therapy by nonsense suppression as suggested by the following statement of Atkinson et al. (see page 1327, 2nd col. 2nd paragraph): "However, *if an effective mechanism for gene therapy by nonsense suppression could one day be developed*, it would then be applicable to similar mutations in a wide range of genes."

The Beier et al. reference, in regards to the correction of deleterious nonsense mutations within human and yeast genomes (see page 4780, concluding paragraph), expressly states that "[A]lthough this is a mostly *unpredictable* and *inefficient* event, the low synthesis of a full-length product *might* be sufficient in special cases to ensure viability of the organism." This statement of Beier et al., contrary to Applicant's assertions clearly conveys to the reader that there is a significant level of unpredictability associated with nonsense mutation suppression by tRNAs.

Applicants further provide a lengthy discussion describing that how one of skill in the art would be able to obtain tRNA sequences from multiple sources and furthermore identify the tRNA sequences of the present invention. However, it is noted that the instant rejection is not centered upon the skilled artisan's inability to make the claimed invention, the instant rejection is

based upon the inability of the skilled artisan to use the claimed invention throughout its entire scope, particularly for *in vivo* therapeutic use.

Double Patenting

5. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

6. Claim 19 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 18 of prior U.S. Patent No. US 6,309,830 B1. This is a double patenting rejection. Claim 19 of the instant application, and issued claim 18 are both specifically limited to the vector pH*hargsup* $tRNA^{Opal}$.

Specification/Sequence Rules

7. The description of Figure 2A does not include a sequence identifier for the tRNA structure set forth in this figure, nor does the Sequence Listing include a sequence identifier which corresponds to this structure, although SEQ ID NO: 14 discloses the mutated form of the tRNA structure. Figure 10 discloses 4 nucleotide sequences, and the description of this figure recites (SEQ ID NO: 5-8). However, the correct sequences should be SEQ ID NO: 7-10. The description of Figure 11 makes reference to SEQ ID NO: 9, however the description should be amended to recite SEQ ID NO: 11. The description of Figure 12 should be modified by replacing SEQ ID NO: 10 with SEQ ID NO: 12. The description of Figure 13 should be modified by

replacing SEQ ID NO: 11 with SEQ ID NO: 13. The description of Figure 14 should be modified by replacing SEQ ID NO: 10 with SEQ ID NO: 14.

Conclusion

8. Claims 1-7, 14-18, and 20-21 are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Patent Examiner
Art Unit 1635

JLE